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Catalyst Pharmaceuticals, Inc. and SERB SA

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

CATALYST PHARMACEUTICALS, Inc., and SERB SA, Plaintiffs, v. JACOBUS PHARMACEUTICALS, INC., Defendant.	Case No. _____ **DEMAND FOR JURY TRIAL**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Catalyst Pharmaceuticals, Inc. ("Catalyst") and SERB SA ("SERB", and collectively "Plaintiffs"), for their Complaint against Defendant Jacobus Pharmaceutical Company, Inc. ("Jacobus"), hereby allege as follows:

NATURE OF THIS ACTION

1. This is a civil action for infringement of U.S. Patent No. 10,793,893 ("the '893 patent"). This action arises under the Patent Laws of the United States, 35 U.S.C. §100, *et seq.*

PARTIES

2. Plaintiff Catalyst is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 355 Alhambra Circle, Suite 1250, Coral Gables, Florida 33134. Catalyst is a commercial-stage biopharmaceutical company focused on developing and commercializing innovative therapies for people with rare debilitating, chronic neuromuscular and neurological diseases.

3. Plaintiff SERB is a corporation organized and existing under the laws of Belgium with its principal place of business at 480 Avenue Louise, Brussels, 1050 Belgium. SERB is the owner by assignment of the ’893 patent.

4. SERB has standing to sue because it is the owner by assignment of the ’893 patent.

5. Catalyst is the exclusive licensee of the ’893 patent and holds substantial rights in the ’893 patent, including (1) the exclusive right to commercialize the ’893 patent in the United States, (2) the right to enforce the ’893 patent against infringement by third-parties, (3) the right to sublicense the ’893 patent, and (4) the right to control prosecution of the ’893 patent and all related patent applications.

6. Catalyst has standing to sue because it holds the right by license to enforce the ’893 patent.

7. On information and belief, Jacobus is a New Jersey corporation having a place of business at 37 Cleveland Lane, Princeton, New Jersey 08540.

8. On information and belief, Jacobus’s registered agent with the state of New Jersey is Laura Jacobus, 37 Cleveland Lane, PO Box 5290, Princeton, NJ 08543.

JURISDICTION AND VENUE

9. This Court has subject-matter jurisdiction over Catalyst's patent infringement claims under 28 U.S.C. §§ 1331 and 1338(a).

10. This Court has personal jurisdiction over Jacobus at least because Jacobus resides in the State of New Jersey as it is both a New Jersey corporation and has a principal place of business in New Jersey. Jacobus also has systematic and continuous contacts with the State of New Jersey. On information and belief, Jacobus is registered with the State of New Jersey's Division of Revenue and Enterprise Services as a business operating in New Jersey under Business No. 0100037836. On information and belief, Jacobus is registered with the State of New Jersey's Department of Health as a drug "manufacturer and wholesaler" under Registration No. 5001409. On information and belief, Jacobus has employees in New Jersey facilities, including at 31 Schalks Crossing Road, Plainsboro, NJ 08536, and at 37 Cleveland Lane, Princeton, New Jersey 08540.

11. On information and belief, Jacobus regularly and continuously transacts business within New Jersey, including by making pharmaceutical products for sale in New Jersey and selling pharmaceutical products in New Jersey. On information and belief, Jacobus manufactures, distributes, offers for sale, and sells Ruzurgi® throughout the United States, including this District. On information and belief, Jacobus purposefully has conducted and continues to conduct business, directly or through its agents and affiliates, in this District, and this District is a likely destination of Ruzurgi®.

12. On information and belief, Jacobus derives substantial revenue from selling pharmaceutical products throughout the United States, including this District, including from the sale of Ruzurgi®. On information and belief, Jacobus derives substantial revenue from the sale

of those products in New Jersey and has availed itself of the privilege of conducting business in New Jersey.

13. On information and belief, Jacobus intends to engage in a future course of conduct that includes continuing acts of patent infringement in New Jersey. These acts will lead to foreseeable harm and injury to Plaintiffs in this District and throughout the United States. For example, Jacobus will continue to manufacture, market, offer for sale, sell, and distribute pharmaceutical products, including Ruzurgi®, throughout the United States, including in New Jersey, prior to the expiration of the patent-in-suit.

14. Venue is proper in this District under 28 U.S.C. §§ 1400(b) at least because Jacobus resides in this District and also has a regular and established place of business in this District and because, on information and belief, Jacobus has induced acts of patent infringement in this District by making, marketing, distributing, and shipping into this District, or by using, distributing, offering to sell, or selling, or by causing others to use, offer to sell, or sell in this District.

LEMS AND CATALYST'S FIRDAPSE® PRODUCT

15. Lambert-Eaton Myasthenic Syndrome ("LEMS") is a rare and debilitating neuromuscular disorder involving impairment of neuromuscular transmission and serious muscle weakness. Clinically, LEMS is characterized by proximal muscle weakness and fatigability, hyporeflexia, or areflexia, and symptoms of autonomic dysfunction such as impotence, dry mouth, and constipation. Other symptoms may include paresthesias, diplopia, and orthostatic hypotension.

16. The neuromuscular symptoms in patients with LEMS typically develop after 40 years of age with a peak incidence between 50 and 70 years of age. Although the exact prevalence of LEMS in the general population is unknown, it has been estimated to affect approximately 1 in 100,000 people. The diagnosis of LEMS can be challenging since the clinical presentation of sub-

acute progressive fatigue and weakness is unspecific. As a result, diagnosis of LEMS is often delayed for months to decades, and is often misdiagnosed for other diseases such as myasthenia gravis, which is characterized by weakness and rapid fatigue of muscles.

17. Amifampridine, also known as 3,4-diaminopyridine or 3,4-DAP, is a nonspecific voltage-dependent potassium channel blocker. Amifampridine blocks the presynaptic voltage-gated potassium channels resulting in a prolonged action potential and increased influx of calcium, which facilitates the release of acetylcholine from the motor nerve terminal and improves neuromuscular transmission.

18. Catalyst holds New Drug Application ("NDA") No. 208078 for the use of amifampridine tablets, which it sells under the trade name Firdapse®. Catalyst's Firdapse® product received FDA approval on November 28, 2018, and was the first product that FDA approved for the treatment of LEMS based on clinical data demonstrating safety and efficacy. Prior to its approval, Firdapse® received breakthrough therapy designation and orphan drug designation from the FDA.

19. Prior to FDA approval of Firdapse®, amifampridine was available in the United States only as an investigational drug product in clinical studies or under the FDA's Expanded Access program, which provides a pathway for a patient to gain treatment to an investigational medical product outside of clinical trials when no comparable or satisfactory alternative therapies are available. No pharmaceutical company, including Jacobus, could lawfully market amifampridine for any indication prior to the approval of Firdapse® as nobody prior to Catalyst had conducted and submitted the pre-clinical and clinical work necessary to obtain FDA approval.

THE '893 PATENT

20. The inventors of the '893 patent discovered that amifampridine undergoes 3-*N*-acetylation to form a single major circulating inactive metabolite that subsequently undergoes renal elimination. The inventors also discovered that the acetylation rate of amifampridine varied significantly depending on certain genetic polymorphisms. The inventors further discovered that amifampridine could be more safely and efficaciously administered by taking into account the individual differences in acetylation rates among patients treated with amifampridine-sensitive diseases.

21. On October 6, 2020, the United States Patent and Trademark Office duly and legally issued the '893 patent, titled "Methods of Administering 3,4-Diaminopyridine." Each and every claim of the '893 patent is valid and enforceable. A true and correct copy of the '893 patent is attached as Exhibit 1.

22. Claim 1 of the '893 patent recites:

> A method of treating a human patient diagnosed with a 3,4-diaminopyridine (3,4-DAP) sensitive disease in need of treatment thereof comprising administering a dose of about 2.5 mg to about 30 mg of 3,4-DAP or a pharmaceutically acceptable salt thereof to a human patient who is a slow acetylator having an N-acetyl transferase 2 (NAT2) gene comprising: a C282T mutation on both alleles of the NAT2 gene; a T341C mutation on both alleles of the NAT2 gene; or a C282T mutation on one allele of the NAT2 gene and a T341C mutation on the other allele of the NAT2 gene or genotype.

(Exhibit 1, at 85.)

JACOBUS' RUZURGI® PRODUCT

23. On information and belief, Jacobus supplied amifampridine for use as an investigation drug product in connection with various physician-held expanded access Investigational New Drug applications ("INDs"). In October 1997, Jacobus submitted its own IND No. 054313 to FDA in order to allow Jacobus to conduct its own amifampridine clinical

development program. On information and belief, Jacobus did not conduct all of the necessary clinical or safety studies to gain FDA approval to market an amifampridine product until after Jacobus learned of SERB's efforts to develop a commercial, amifampridine product for the United States market.

24. Between 1993 and 2010, Jacobus supplied a limited number of patients with an amifampridine product on an investigational basis.

25. Jacobus met and communicated several times with FDA officials in connection with Jacobus' amifampridine development program, including on at least September 7, 2010, June 17, 2017, and February 17, 2016.

26. Attached as Exhibit 2 is a true and correct copy of certain administrative correspondence between Jacobus and FDA pertaining to Jacobus's amifampridine development program.

27. At the June 17, 2014 meeting between Jacobus and FDA, FDA informed Jacobus that: "You need to perform further *in vitro* studies to characterize the enzyme responsible for the metabolism of 3,4-DAP. N-acetyltransferase 2 (NAT2) is known to be involved in the N-acetylation metabolism of some drugs. If you confirm that NAT2 is the major enzyme responsible for 3,4-DAP metabolism, you need to characterize the impact of NAT2 status (rapid metabolizers vs. slow metabolizers) on PK and clinical responses of 3,4-DAP." (Ex. 2, at 44 (Meeting Minutes, Type B, End-of Phase 2 Meeting, June 17, 2014).)

28. On information and belief, FDA's guidance and instruction to Jacobus was derived from confidential information obtained provided by a predecessor-in-interest to Catalyst and based on the work of the inventors of the '893 patent.

29. On information and belief, prior to June 17, 2014, Jacobus was not aware that amifampridine was a substrate for the NAT enzyme despite having manufactured amifampridine for investigational use for nearly 14 years and despite having spent many years pursuing its own amifampridine clinical development program.

30. Despite FDA's admonition to Jacobus that the NAT2 enzyme may be the major enzyme responsible for metabolism of amifampridine, Jacobus did not appreciate the impact of the metabolic activity on the safe and efficacious administration of amifampridine, and instead told FDA that "[it] did not consider information about NAT status is [sic] useful for dosing recommendations." (Ex. 2, at 45 (Meeting Minutes, Type B, End-of Phase 2 Meeting, June 17, 2014).

31. On December 5, 2017, Jacobus submitted NDA No. 209321 to FDA seeking approval to market an amifampridine product under the name Ruzurgi®. FDA refused to file Jacobus' NDA because it lacked sufficient information to permit a substantive review.

32. On June 15, 2018, Jacobus re-submitted NDA No. 209321 with additional information not previously provided to FDA.

33. On May 6, 2019, FDA approved Jacobus' NDA 209321 for the treatment of LEMS in pediatric patients who were between 6 and 17 years of age.

34. On information and belief, Exhibit 3 is a true and correct copy of the current FDA-approved Prescribing Information for Ruzurgi® ("Ruzurgi® Prescribing Information").

35. Despite Jacobus' statements to FDA on June 15, 2014, "[it] did not consider information about NAT status is [sic] useful for dosing recommendations," the Ruzurgi® Prescribing Information contains extensive information that promotes using NAT2 status to administer amifampridine to patients.

36. The "Dosage and Administration" section of the Ruzurgi® Prescribing Information promises, encourages, and directs health care providers: "The recommended starting dosage of RUZURGI in pediatric patients weighing 45 kg or more who are known N-acetyltransferase 2 (NAT2) poor metabolizers is 15 mg daily taken orally in divided doses. The recommended starting dosage in pediatric patients weighing less than 45 kg who are known NAT2 poor metabolizers is 7.5 mg daily taken orally in divided doses." (Ex. 3, at 3.)

37. The "Use in Specific Populations" section of the Ruzurgi® Prescribing Information further promotes: "Exposure of RUZURGI is increased in patients who are N-acetyltransferase 2 (NAT2) poor metabolizers … Therefore, initiate RUZURGI in patients who are known NAT2 poor metabolizers at the lowest recommended starting dosage and monitor for adverse reactions … Consider dosage modification of RUZURGI for patients who are known NAT2 poor metabolizers as needed based on clinical effect and tolerability." (Ex. 3, at 7.)

38. The "Pharmacogenomics" section of the Ruzurgi® Prescribing Information further promotes: "Genetic variants in the N-acetyltransferase gene 2 (NAT2) affect the rate and extent of RUZURGI metabolism. In normal healthy volunteers, poor metabolizers, also referred to as "slow acetylators" (i.e., carriers of two reduced function alleles) had higher average plasma amifampridine concentrations than intermediate metabolizers, also referred to as "intermediate acetylators" (i.e., carriers of one reduced and one normal function alleles), and normal metabolizers, also referred to as "fast/rapid acetylators" (i.e., carriers of two normal function alleles)." (Ex. 3, at 11.) It further states that, within the general population, the "NAT2 poor metabolizer phenotype prevalence is 40-60% in the White and African American populations, and in 10-30% in Asian ethnic populations." (*Id.*)

39. On information and belief, physicians prescribing Ruzurgi® have administered, and will continue to administer, the drug to patients with LEMS who are slow acetylators of amifampridine, including patients having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele.

40. On information and belief, Jacobus knows that healthcare providers have and will continue to administer Ruzurgi® to patients with LEMS who are slow acetylators of amifampridine, including patients having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele, in accordance with the dosing guidance contained on the Ruzurgi® Prescribing Information.

41. On information and belief, Jacobus intends for Ruzurgi® to be administered to patients with LEMS who are slow acetylators of amifampridine, including patients having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele, in accordance with the Prescribing Information for Ruzurgi®.

42. On information and belief, Jacobus operates a website with the address www.ruzurgi.com ("the Ruzurgi website"). The Ruzurgi website promotes and encourages the administration of Ruzurgi to patients with LEMS who are slow acetylators of amifampridine.

43. On information and belief, Jacobus markets the amifampridine product that is the subject of NDA No. 209321 under the brand name Ruzurgi®. The average retail price of Ruzurgi® is approximately $175,000 per patient per year before any applicable discounts.

COUNT I: INFRINGEMENT OF '893 PATENT

44. Plaintiffs incorporate by reference paragraphs 1-43 as if fully set forth herein.

45. On information and belief, Jacobus has been and is now actively inducing infringement of at least claim 1 of the '893 patent in violation of 35 U.S.C. §271(b) by marketing, promoting, offering for sale, and selling Ruzurgi® for use by patients with LEMS who are slow acetylators of amifampridine.

46. Prior to the filing of this Complaint, Catalyst notified Jacobus by letter sent both electronically and by overnight delivery of the existence of the '893 patent and of the infringing uses of Ruzurgi®. As a result, Jacobus had actual knowledge of the existence of the '893 patent and of its infringing activities by at least its receipt of Catalyst's notice before filing this Complaint.

47. On information and belief, Jacobus has knowledge of the '893 patent and of the infringing use of Ruzurgi® at least as of the filing and/or service of this Complaint.

48. On information and belief, Jacobus intends for healthcare providers to administer Ruzurgi® to patients in accordance with the Ruzurgi® Prescribing Information, including the safety information and other conditions of use provided on the Ruzurgi® Prescribing Information, and intends for patients to take Ruzurgi® in accordance with instructions from their healthcare providers and the Ruzurgi® Prescribing Information.

49. The Ruzurgi® Prescribing Information directs, encourages, and promotes the treatment of an amifampridine-sensitive disease, LEMS, by administering a dose between about 2.5 mg to about 30 mg of amifampridine to patients who are slow acetylators of amifampridine, having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele.

50. On information and belief, healthcare providers have administered and will continue to administer Ruzurgi® to patients who are slow acetylators of amifampridine, having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele.

51. On information and belief, healthcare providers will directly infringe the method of at least claim 1 of the '893 patent when administering Ruzurgi® to patients who are slow acetylators, including patients who are slow acetylators of amifampridine, having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele.

52. On information and belief, patients who are slow acetylators, including patients who are slow acetylators of amifampridine, having an NAT2 gene with a C282T mutation on both alleles, a T341C mutation on both alleles, or a C282T mutation on one allele and a T341C mutation on the other allele, will directly infringe the method of at least claim 1 of the '893 patent when taking Ruzurgi® in accordance with their healthcare providers' instructions and the Ruzurgi® Prescribing Information.

53. On information and belief, Jacobus actively induces infringement of at least claim 1 of the '893 patent because it knows and intends for healthcare providers and patients to infringe the method of at least claim 1 when following the instructions on the Ruzurgi® Prescribing Information.

54. On information and belief, Jacobus' continuing infringement of the '893 patent occurs with full knowledge of the '893 patent and without a reasonable basis for believing that it does not infringe the '893 patent.

55. As a direct and proximate result of Jacobus' infringement of the '893 patent, Plaintiffs have suffered and will continue to suffer monetary damages, including lost profits.

56. Plaintiffs are entitled to recover from Jacobus the damages sustained by Plaintiffs as a result of Jacobus' wrongful acts in an amount to be determined at trial.

57. Jacobus' acts of infringement of the '893 patent will continue unless enjoined by the Court.

58. Unless Jacobus' infringing activities are enjoined by the Court, Plaintiffs have been and will continue to be substantially and irreparably harmed for which there is no adequate remedy at law. Accordingly, Plaintiffs are entitled to preliminary and/or permanent injunction against further infringement.

59. On information and belief, Jacobus' infringement of the '893 patent has been and continues to be willful. Jacobus' conduct with respect to the '893 patent renders this case "exceptional" as that term is set forth in 35 U.S.C. §285, and entitles Plaintiffs to recovery of their attorneys' fees and such other relief as this Court deems proper.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment in their favor as follows:

A. Declare that Jacobus has induced infringement of the '893 patent;

B. Preliminarily and permanently enjoin Jacobus and their officers, employees, and all persons acting in concert or in privity with them, from infringing the '893 patent until the expiration of the '893 patent (including any exclusivities or extensions to which Plaintiffs are or become entitled), and for all further and proper injunctive relief pursuant to 35 U.S.C. § 283;

C. Award to Plaintiffs such past damages in the form of lost profits or a reasonable royalty that is adequate to fully compensate Plaintiffs for Jacobus' infringement of the '893 patent;

D. Declare that Plaintiffs' infringement has been willful, wanton, and deliberate and that the damages against it be increased up to treble on this basis or for any other basis in accordance with the law;

E. Declare this case is "exceptional" and an award to Plaintiffs of their costs and reasonable attorneys' fees, as provided by 35 U.S.C. §285; and

F. Grant Plaintiffs such further and other relief as the Court may deem proper and just.

DEMAND FOR JURY TRIAL

Plaintiffs demand a jury trial on all issues so triable.

Dated: October 16, 2020

Respectfully submitted,

s/Liza M. Walsh

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LOCAL RULE 11.2 CERTIFICATION

I hereby certify that, to the best of my knowledge, the matter in controversy is not the subject of any other pending or anticipated litigation in any court or arbitration proceeding, nor are there any non-parties known to Plaintiffs that should be joined to this action. In addition, I recognize a continuing obligation during the course of this litigation to file and to serve on all other parties and with the Court an amended certification if there is a change in the facts stated in this original certification.

Dated: October 16, 2020

Respectfully submitted,

s/ Liza M. Walsh

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LOCAL RULE 201.1 CERTIFICATION

I hereby certify that the above-captioned matter is not subject to compulsory arbitration in that the Plaintiffs seek, inter alia, injunctive relief.

Dated: October 16, 2020

Respectfully submitted,

s/ Liza M. Walsh

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TABLE OF EXHIBITS

EXHIBIT 1	U.S. Patent No. 10,793,893
EXHIBIT 2	Ruzurgi® FDA Administrative and Correspondence Documents
EXHIBIT 3	Ruzurgi® Prescribing Information (April 2020 revision)